

## **REMARKS**

### **Status of the Claims**

Claims 5, 6 and 20 as previously pending were appealed to the Board of Patent Appeals (Appeal No. 2006-3085). In a Decision dated May 30, 2007, the Examiner's rejections were reversed and a new ground of rejection based on 35 U.S.C. § 103 was set forth. See, Decision on Appeal, pages 12-15.

Pursuant to 37 C.F.R. § 41.50(b), Applicants submit the foregoing amendments and following remarks for reconsideration by the Examiner.

Claim 5 has been amended as shown above to clarify that the zinc fingers of each fusion protein bind to DNA in a sequence-specific manner (see, e.g., page 1, lines 11-12) and that the fusion proteins are joined via the zinc fingers (see, e.g., FIG. 3B). Thus, claims 5, 6 and 20 are pending as shown above.

### **35 U.S.C. 103**

Previous appealed claims 5, 6 and 20 were newly rejected by the Board under 35 U.S.C. § 103(a) as allegedly obvious over Pomerantz (1988) *Biochemistry* 37(4):965-970 (hereinafter "Pomerantz") in view of Krylov et al. (1994) *EMBO J.* 13(12):2849-2861 (hereinafter "Krylov"). See, Board Decision on Appeal, pages 12-15. Pomerantz was cited for disclosing a zinc finger protein fused to a naturally occurring dimerization domain extracted from the GAL4 protein and for suggesting the use, including citation of various references, of non-naturally occurring dimerization domains. *Id.* Krylov, reference 19 of Pomerantz, was cited for demonstrating that non-naturally occurring peptide linkers could be utilized to complex zinc fingers. *Id.*

In view of the foregoing amendments and following remarks, Applicants submit that the claims are non-obvious over the cited references.

The Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 (U.S. Apr. 30, 2007) reaffirmed the viability of the four factual inquiries underlying an obviousness analysis provided in *Graham v. John Deere*, 148 USPQ 459, 467 (U.S. 1966). These factors include: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary considerations.

Moreover, the Supreme Court in *KSR* recognized that the “teaching, suggestion, or motivation” analysis provides a helpful insight in determining whether the claimed subject matter is obvious. This analysis is provided in MPEP § 2142. In particular, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Additionally, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. As noted by the Board in their Decision on Appeal, the teaching or suggestion to make the claimed combination, as well as the reasonable expectation of success, must be found in the prior art, not in applicant’s disclosure. See, e.g., *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), also cited on page 13 of the Board’s Decision on Appeal. In view of the law regarding obviousness, Applicants respectfully submit the claims as pending are not obvious over Pomerantz and Krylov.

The pending claims are drawn to complexes comprising two or more fusion proteins. Each fusion protein includes a zinc finger protein that binds to DNA in a sequence-specific manner. Furthermore, the zinc finger proteins in each fusion are linked using a non-naturally occurring peptide linker. Pomerantz and Krylov do not teach or suggest such complexes. Krylov is completely silent as to zinc finger proteins, disclosing only leucine zipper and helix loop helix proteins. As was known in the art at the time of filing and noted throughout the specification, zinc finger proteins (as claimed) do not contain leucine zipper or HLH motifs characteristic of the proteins as disclosed in Kylov. See, e.g. Section II of the specification starting at page 14, line 11.

For its part, Pomerantz relates to fusions of zinc finger proteins with GAL4. Unlike the claimed complexes in which each component of the fusion protein comprises a zinc finger protein that binds to DNA in a sequence-specific manner, Pomerantz explicitly teaches that the GAL4 element does not bind to DNA in a sequence specific manner (see, page 967, right column of Pomerantz, emphasis added):

The utility of this zinc finger-GAL4 fusion rests on the expectation that specificity will be determined primarily by the zinc fingers, which can be designed or selected to recognize desired target sites. **Although the GAL4**

**linker and dimerization element contact DNA, they do not make any base-specific contacts in the crystal structure** (18). Binding studies with ZFGD1 confirmed that the central 13 base-pair region of this site, **where the GAL4 linker and dimerization elements are expected to contact the DNA (Figure 1), makes little contribution to sequence-specific recognition.**

Indeed, Pomerantz clearly indicates that GAL4 was fused to a zinc finger protein in order to enhance the affinity and specificity of its fusion zinc finger protein partner (page 966, left column of Pomerantz, emphasis added):

The GAL4 domain was chosen because structural information is available for this domain (18) and because it contains a coiled-coil motif, a **simple**, well-understood structure that can be further modified for design purposes. **The GAL4 dimerization motif is also interesting because it docks to DNA and presumably would help to position and orient the fused zinc finger domains. Moreover, the dimerization motif does not appear to require specific sequences for binding.**

Thus, Pomerantz teaches away from complexes as claimed comprising two zinc finger proteins that each bind to DNA in a sequence-specific manner and wherein the zinc finger proteins are linked by a non-naturally occurring peptide. Pomerantz clearly chose not to form fusions of zinc finger proteins because their binding to their target sites was specific and because using two sequence-specific binding zinc finger proteins as claimed would not be a “simple” structure like Pomerantz’s fusions containing the GAL4 dimerization domain. (See, passage of Pomerantz reproduced above). Therefore, there is no motivation in Pomerantz or Krylov, or any combination of Pomerantz and Krylov to form complexes of two zinc finger proteins, each zinc finger protein binding specifically to DNA and linked via a non-naturally occurring peptide linker.

When the references are considered as a whole for what they fairly teach, there are several elements missing from the combination. As stated in *KSR*, “a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, page 14. Here, as explained above, less than all of the elements are set forth in the stated combination and, moreover, the primary reference teaches

away from complexes of DNA-binding zinc finger proteins linked by non-naturally occurring linkers.


**CONCLUSION**

Applicants believe that the claimed subject matter is now in condition for allowance and early notification to that effect is respectfully requested. If any issues remain to be addressed, the Examiner is encouraged to telephone the undersigned.

Please address all correspondence to the undersigned.

Respectfully submitted,

Date: July 11, 2007

By:   
Dahna S. Pasternak  
Registration No. 41,411  
Attorney for Applicant

ROBINS & PASTERNAK LLP  
1731 Embarcadero Road, Suite 230  
Palo Alto, CA 94303  
Tel.: (650) 493-3400  
Fax: (650) 493-3440